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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

	Application No.	Applicant(s)		
	10/534,978	LI ET AL.		
Office Action Summary	Examiner	Art Unit		
	David C. Thomas	1637		
The MAILING DATE of this communication app Period for Reply	ears on the cover sheet with the c	orrespondence address		
A SHORTENED STATUTORY PERIOD FOR REPLY WHICHEVER IS LONGER, FROM THE MAILING DA  - Extensions of time may be available under the provisions of 37 CFR 1.13 after SIX (6) MONTHS from the mailing date of this communication.  - If NO period for reply is specified above, the maximum statutory period w  - Failure to reply within the set or extended period for reply will, by statute, Any reply received by the Office later than three months after the mailing earned patent term adjustment. See 37 CFR 1.704(b).	ATE OF THIS COMMUNICATION 36(a). In no event, however, may a reply be tim vill apply and will expire SIX (6) MONTHS from cause the application to become ABANDONE	N. sely filed the mailing date of this communication. D (35 U.S.C. § 133).		
Status	•			
Responsive to communication(s) filed on 15 Au     This action is <b>FINAL</b> . 2b) ☐ This     Since this application is in condition for allowar closed in accordance with the practice under E	action is non-final.  nce except for formal matters, pro			
Disposition of Claims				
4)  Claim(s) 1-20 is/are pending in the application. 4a) Of the above claim(s) 16-19 is/are withdraw 5)  Claim(s) is/are allowed. 6)  Claim(s) 1-15 and 20 is/are rejected. 7)  Claim(s) is/are objected to. 8)  Claim(s) are subject to restriction and/or	n from consideration.			
Application Papers		·		
9) The specification is objected to by the Examiner 10) The drawing(s) filed on is/are: a) access applicant may not request that any objection to the Replacement drawing sheet(s) including the correction of the original transfer of the second sheet (s) including the correction.  11) The oath or declaration is objected to by the Examiner  9)	epted or b) objected to by the liderawing(s) be held in abeyance. See ion is required if the drawing(s) is obj	e 37 CFR 1.85(a). jected to. See 37 CFR 1.121(d).		
Priority under 35 U.S.C. § 119				
<ul> <li>12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).</li> <li>a) All b) Some * c) None of:</li> <li>1. Certified copies of the priority documents have been received.</li> <li>2. Certified copies of the priority documents have been received in Application No</li> <li>3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).</li> <li>* See the attached detailed Office action for a list of the certified copies not received.</li> </ul>				
Attachment(s)  1) Notice of References Cited (PTO-892)  2) Notice of Draftsperson's Patent Drawing Review (PTO-948)  3) Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 13 June 2007.	4) Interview Summary Paper No(s)/Mail Da 5) Notice of Informal P 6) Other:	ate		

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#### **DETAILED ACTION**

1. Applicant's amendment filed August 15, 2007 is acknowledged. Claims 8, 11 and 20 (currently amended) and claims 1-7, 9, 10 and 12-15 (original) will be examined on the merits. Claims 16-19 were previously withdrawn.

## Claim Rejections - 35 USC § 103

- 2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:
  - (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
- 3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).
- 4. Claims 1-6, 8-13 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harley et al. (U.S. Patent No. 5,891,639) in view of Elmore et al. (Diagn. Mol. Pathol. (2002) 11:177-185).

With regard to claims 1, 5 and 13, Harley teaches a method for detecting and quantifying telomerase activity in a biological sample (for overview, see column 2, line 63 to column 3, line 18), the method comprising the steps of:

adding the biological sample to a reaction tube (cell extract is added to tube containing reaction components, column 28, lines 36-44) comprising:

a first reaction mixture comprising a first primer and nucleoside triphosphates (telomerase primer (TS) and other reaction components including dNTPs are added to tube prior to sample addition, column 28, lines 36-44);

a second reaction mixture comprising a second primer and a DNA polymerase (second primer or polymerase is added under a wax layer, column 11, lines 25-30 and column 28, lines 17-20); and

a wax layer separating the first reaction mixture from the second reaction mixture in the reaction tube (wax layer is used to separate telomerase extension reaction from the amplification reaction, and thus components such as the polymerase or second primer of the amplification reaction are separated the extension reaction components until after the telomerase reaction, column 11, lines 23-30 and column 28, lines 13-17);

incubating the biological sample with the first reaction mixture under conditions suitable for a telomerase to produce an extension product from the first primer, said extension product having a 3' end (telomerase extension reaction is performed for 10 minutes at 20°C to allow TS primer extension, column 28, lines 47-48);

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admixing the extension product with the second reaction mixture by melting the wax layer (sample tubes were transferred to a thermocycler to begin cycling, with the wax layer melting upon temperature reaching 70 °C, column 28, lines 47-54);

amplifying the extension product using polymerase chain reaction under conditions that allow the detection of telomerase activity from a single 293T cell (samples are subjected to thermocycling to amplify the extension products, column 28, lines 50-52; the assay can be sensitive down to a single cell, column 43, lines 44-46 and column 44, lines 15-19), and

quantifying the amplified extension product using a control template (an internal control nucleic acid can be added to the reaction mixture in known amounts and amplified with different primers than used for the telomerase-extended substrate, column 14, lines 45-52).

With regard to claim 2, Harley teaches a method wherein the biological sample is added in the form of a cell or tissue extract (cell extract is added to tube containing reaction components, column 28, lines 36-44 and column 34, lines 1-37).

With regard to claim 3, Harley teaches a method wherein the polymerase chain reaction is detected by using a fluorescently labeled probe oligonucleotide that binds to a sequence between the first and the second primers (products extended by telomerase and amplified can be detected with TaqMan probes which hybridizes to internal site between primers, column 15, lines 26-32 and column 41, lines 45-54).

With regard to claim 4, Harley teaches a method wherein the real-time polymerase chain reaction is performed in the presence of a fluorescent dye that binds

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preferentially to double-stranded DNA (detection of telomerase-extended substrates or amplification products can be performed with SYBR Green dye, which exhibits enhanced fluorescence when bound to double-stranded nucleic acids, column 21, lines 20-24 and 35-40).

With regard to claim 6, Harley teaches a method further comprising:

elongating the extended product at the 3' end by one of polyadenylation and ligation (extension of telomerase primer can be performed with DNA ligase and can be extended multiple times, column 9, lines 37-52) or a combination of a ligase and polymerase can be used to amplify the extension products (Harley, column 17, lines 49-51).

With regard to claim 8, Harley teaches a method for detecting and quantifying telomerase activity in a sample cell (detection of telomerase in situ, column 3, lines 23-26), the method comprising the steps of:

suspending the sample cell in a cell suspension (single cells can be obtained by various means, such as by serial dilutions or by using a cell sorter, either of which results in suspension of the cell in a suspension prior to performing the telomerase detection steps, column 43, lines 44-49; cells will also be suspended by drawing tumor tissue through a fine needle, in order to test the tumor biopsy for telomerase activity, column 24, lines 26-30);

passing the cell suspension through a needle at least once (fine needle aspirates used to biopsy tumor tissue, column 24, lines 26-30);

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introducing into a sample cell a first primer and nucleoside triphosphates (telomerase substrate in form of plasmid containing TS sequence is internalized in cell, column 36, line 56 to column 37, line 7; cells are permeabilized to allow for detection by PCR using dNTPS and Taq polymerase, column 37, lines 42-45 and line 62 to column 38, line 16);

incubating the sample cell under conditions suitable for a telomerase to produce an extension product from the first primer (cells are incubated after internalization of substrate, column 37, lines 29-31);

amplifying the extension product using polymerase chain reaction (PCR condition are established after permeabilization, column 37, line 62 to column 38, line 16); and

quantifying the amplified extension product using a control template (an internal control nucleic acid can be added to the reaction mixture in known amounts and amplified with different primers than used for the telomerase-extended substrate, column 14, lines 45-52).

With regard to claim 9, Harley teaches a method further comprising:

lysing the sample cell with a lysis buffer (after incubation with the internalized substrate, cells are treated with proteases to permeabilize the cells, column 37, lines 55-60).

With regard to claim 10, Harley teaches a method wherein the first primer is introduced into the sample cell (internalization of substrate is achieved using passive internalization, microporation, or electroporation, column 37, lines 20-31).

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With regard to claim 11, Harley teaches a method wherein the first primer is introduced into the sample cell by a procedure comprising:

culturing the cell in a culture medium containing the first primer (substrate is electroporated into cells placed in DMEM media, column 37, lines 26-29).

With regard to claim 12, Harley teaches a method wherein the polymerase chain reaction is performed in the presence of a fluorescent dye that binds preferentially to double-stranded DNA (detection of telomerase-extended substrates or amplification products can be performed with SYBR Green dye, which exhibits enhanced fluorescence when bound to double-stranded nucleic acids, column 21, lines 20-24 and 35-40).

With regard to claim 15, Harley teaches a method for detecting and quantifying telomerase activity in a biological sample, the method comprising the steps of:

adding the biological sample to a reaction tube (cell extract is added to tube containing reaction components, column 28, lines 36-44) comprising:

a first reaction mixture comprising a first primer and nucleoside triphosphates (telomerase primer (TS) and other reaction components including dNTPs are added to tube prior to sample addition, column 28, lines 36-44);

a second reaction mixture comprising a second primer and a DNA polymerase (second primer or polymerase is added under a wax layer, column 11, lines 25-30 and column 28, lines 17-20); and

a wax layer separating the first reaction mixture from the second reaction mixture in the reaction tube (wax layer is used to separate telomerase extension reaction from

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the amplification reaction, and thus components such as the polymerase or second primer of the amplification reaction are separated the extension reaction components until after the telomerase reaction, column 11, lines 23-30 and column 28, lines 13-17);

incubating the biological sample with the first reaction mixture under conditions suitable for a telomerase to produce an extension product from the first primer, said extension product (telomerase extension reaction is performed for 10 minutes at 20°C to allow TS primer extension, column 28, lines 47-48);

elongating the extended product at a 3' end by one of polyadenylation and ligation (extension of telomerase primer can be performed with DNA ligase and can be extended multiple times, column 9, lines 37-52);

admixing the extension product with the second reaction mixture by melting the wax layer (sample tubes were transferred to a thermocycler to begin cycling, with the wax layer melting upon temperature reaching 70°C, column 28, lines 47-54);

amplifying the extension product using a polymerase chain reaction under conditions that allow the detection of telomerase activity from a single 293T cell (samples are subjected to thermocycling to amplify the extension products, column 28, lines 50-52; the assay can be sensitive down to a single cell, column 43, lines 44-46 and column 44, lines 15-19); and

quantifying the amplified extension product using a control template (an internal control nucleic acid can be added to the reaction mixture in known amounts and amplified with different primers than used for the telomerase-extended substrate, column 14, lines 45-52),

wherein the second primer comprises a nucleotide sequence that is complementary to the nucleotide sequence at a 3' end of the elongated extension product (second primer, the downstream CX primer, is complementary to sequences at end of the telomerase extension product, column 10, lines 18-24).

Harley does not teach a real-time polymerase chain reaction for *in vitro* and *in situ* analysis. Harley also does not teach a second primer that is a single-labeled fluorogenic primer that produces an increased amount of fluorescence emission when the fluorogenic primer is incorporated into double-stranded polymerase chain reaction product. Harley also does teach a method wherein both the polymerase and second primer are separated from the first reaction mixture by a wax layer.

Elmore teaches a method of quantitative analysis of telomerase activity in breast cancer specimens using real-time PCR (p. 179, column 1, lines 2-7), including the use of a probe labeled with a single fluorogenic compound and a quencher moiety to allow real-time detection (p. 178, column 2, lines 24-27 and Figure 1).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the methods of Harley who teaches a method of detecting telomerase activity using conventional end-point PCR and reaction mixes separated by a wax barrier and those of Elmore who teaches a method of detecting telomerase activity using real-time PCR, since the two reaction-mix approach using a wax barrier is easily adapted to a real-time PCR format. Thus, an ordinary practitioner would have been motivated to combine the methods of Harley and Elmore since the development of a fluorescent real-time assay simplifies the overall assay setup, avoids

the use of radioactivity, and improves accuracy and turnaround time, which are all important factors in clinical tests (Elmore, p. 179, column 2, lines 1-8 and p. 184, column 2, lines 24-50). Furthermore, the in situ assay can also be performed in realtime using a fluorescent primer (Elmore, Figure 1) that can enter permeabilized cells along with other PCR reagents (Harley, column 37, line 62 to column 38, line 16).

Though Harley does not teach a method of sequestering both a polymerase and second primer in a tube under a wax layer, this reference teaches that either reagent can be separated from the other mix in this manner (Harley, column 11, lines 25-30). The purpose of the wax barrier is to separate the telomerase extension reaction from the amplification reaction until after the telomerase extension products are formed, and the removal of either the downstream primer or the polymerase will achieve this. The other reagent can be present in the first mixture since amplification will not occur without both the downstream primer and polymerase present. However, it is obvious that both reagents could be placed under the wax layer since there is no functional reason or obvious advantage to have or not have one of the reagents present in the telomerase mixture. To this end, Harley teaches methods to provide any of the reagents either independently or in a mixture as a liquid or in lyophilized form to improve ease of use, with proper conditions in place to stabilize degradable reagent such as the use of stabilizers (Harley, column 26, lines 10-18). Thus, it would be obvious to an ordinary practitioner that one or both reagents could be separated from the first reaction mixture using a wax barrier.

5. Claims 7 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harley et al. (U.S. Patent No. 5,891,639) in view of Elmore et al. (Diagn. Mol. Pathol. (2002) 11:177-185) and further in view of Choo et al. (GenBank Accession No. AX395585 (2002) and WO 02/04488).

Harley and Elmore together teach the limitations of claims 1-6, 8-13 and 15.

Neither Harley nor Elmore teach a method wherein the control template has a nucleotide sequence recited in SEQ ID NO:2.

With regard to claims 7 and 14, Choo teaches a method wherein the control template has a nucleotide sequence recited in SEQ ID NO:2 (SEQ ID NO:2 is identical to 68-base sequence taught by Choo, TSR8, used as specific control template for telomerase assays, p. 92, line 3 and p. 98, lines 2-4).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the methods of Harley who teaches a method of detecting telomerase activity using conventional end-point PCR and reaction mixes separated by a wax barrier and those of Elmore who teaches a method of detecting telomerase activity using real-time PCR, with those of Choo, who teaches a specific substrate that can serve as a positive control template for quantitation of telomerase activity. Thus, an ordinary practitioner would have been motivated to combine the methods of Harley and Elmore for a two-reaction mix fluorescent real-time assay with a control template that allows quantitation of telomerase assays by running a parallel amplification of a similar target sequence containing eight copies of the telomeric

repeat. The use of such a control template allows the effects of various conditions and inhibitors of the telomerase extension and amplification reactions to be measured.

6. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Harley et al. (U.S. Patent No. 5,891,639) in view of Elmore et al. (Diagn. Mol. Pathol. (2002) 11:177-185) and further in view of Nakamura et al. (J. Cell. Physiol. (2001) 187:392-401).

Harley and Elmore together teach the limitations of claims 1-6, 8-13 and 15, as discussed above.

Neither Harley nor Elmore teach a method for monitoring the effectiveness of treatment of a subject with an agent that inhibits telomerase activity by obtaining a preadministration sample and a post-administration sample from the subject prior to administration of the agent, and comparing the level of telomerase activity in the preadministration sample with the level of telomerase activity in the post-administration sample or samples.

With regard to claim 20, Nakamura teaches a method for monitoring the effectiveness of treatment of a subject with an agent that inhibits telomerase activity (inhibitors of telomerase were tested as therapeutic strategy against human liver cancer cells, p. 393, column 1, lines 15-24), said method comprising:

obtaining a pre-administration sample from the subject prior to administration of the agent and detecting a level of telomerase activity in the pre-administration sample

(cell lines were obtained from human liver cancers, p. 393, column 1, line 61 to column 2, line 8);

detecting the level of telomerase activity in the pre-administration samples (level of telomerase activity was measured in control samples prior to treatment, p. 393, column 2, lines 18-21; controls without treatment are seen as 0 level in Figure 3 and lane 1 of Figure 4A);

detecting the level of telomerase activity in the post-administration samples (level of telomerase activity was measured in treated samples in both dose- and time-dependent manners, p. 395, column 2, lines 5-17); and

comparing the level of telomerase activity in the pre-administration sample with the level of telomerase activity in the post-administration sample or samples (effect of treatment is seen as decrease of telomerase activity with increasing dose and time of treatment compared to control samples, p. 395, column 2, line 17 to p. 397, column 1, line 7 and Figures 3 and 4B).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the methods of Harley who teaches a method of detecting telomerase activity using conventional end-point PCR and reaction mixes separated by a wax barrier and those of Elmore who teaches a method of detecting telomerase activity using real-time PCR, with the methods of Nakamura since Nakamura teaches a method to monitor the effectiveness of treatment of a subject with an agent that inhibits telomerase activity, which can be monitored by the combined methods of Harley and Elmore. Thus, an ordinary practitioner would have been

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motivated to combine the methods of detecting telomerase activity of Harley and Elmore with the methods of monitoring treatment with telomerase-inhibiting agents taught by Nakamura since the development of a fluorescent real-time assay simplifies the overall assay setup, avoids the use of radioactivity, and improves accuracy and turnaround time compared to the traditional gel assay taught by Nakamura, which are all important factors in clinical tests (Elmore, p. 179, column 2, lines 1-8 and p. 184, column 2, lines 24-50). Furthermore, the *in situ* assay can also be performed in real-time using a fluorescent primer (Elmore, Figure 1) that can enter permeabilized cells along with other PCR reagents (Harley, column 37, line 62 to column 38, line 16).

## Response to Arguments

7. Applicant's arguments filed August 15, 2007 have been fully considered but they are not persuasive.

Applicant argues that the rejection of claim 20 under 35 U.S.C. § 102(b) as being anticipated by Nakamura et al. ((J. Cell. Physiol. (2001) 187:392-401) should be withdrawn since the reference no longer teaches all the limitations of the claims as amended. In particular, Applicant argues that Nakamura fails to disclose a method for detecting telomerase activity as recited in claim 1, including the use of a wax layer to separate first and second reaction mixtures. The Examiner agrees that Nakamura does not teach the methods of detecting telomerase activity recited in claim 1 and therefore the 102(b) rejection is withdrawn. However, the methods of Nakamura for monitoring the effectiveness of treatment of a subject with an agent that inhibits telomerase activity is now combined in a 103 rejection of claim 20 with Harley et al. (U.S. Patent No.

5,891,639) in view of Elmore et al. (Diagn. Mol. Pathol. (2002) since the combination of Harley and Elmore teach the limitations of claim 1, as discussed below.

Applicant then argues that the rejection of claims 1-6, 8-13 and 15 under 35 U.S.C. § 103(a) as being obvious over Harley in view of Elmore and the rejection of claims 7 and 14 as being obvious over Harley in view of Elmore and further in view of Choo (GenBank Accession No. AX395585 (2002) and WO 02/04488) should be withdrawn since the references no longer teach all the limitations of the claims as amended. In particular, Applicant argues that none of the cited references teach a method comprising the steps of adding a biological sample to a reaction tube comprising a first reaction mixture comprising a first primer and nucleoside triphosphates, a second reaction mixture comprising a second primer and a DNA polymerase, and a wax layer separating the two reaction mixtures. Applicant further argues that since Harley does not teach a method wherein both the polymerase and the second primer are separated from the first reaction mixture by a wax layer, it would not be obvious to place these two components in the second reaction mixture under the wax layer, even though the Examiner previously cited that the purpose of the wax barrier is to separate telomerase extension reactions and amplification reactions (Harley, column 11, lines 23-25). Consistent with this reasoning, the Applicants also submit that one skilled in the art realizes that the presence of additional primers in a reaction mixture may lead to unexpected results, especially when two reactions are carried out sequentially in the same tube. Furthermore, Harley teaches methods wherein reaction components such as the primer or polymerase could be sequestered

under the wax layer (column 11, lines 25-30) and also teaches that one or more components can be provided in liquid or lyophilized form for ease of use, indicating that at least two components can be placed in solution in different positions in the kit. Therefore, an ordinary practitioner would realize that both the primer and polymerase could be placed under the wax, since Harley teaches that these components can be individually placed under the wax to separate them from the extension reaction, and that for ease of use, multiple components can be placed together.

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Applicant then argues that none of the cited references teach a method as cited in claim 8, comprising the steps of suspending the sample cell in a cell suspension and passing the cell suspension through a needle at least once. Though there are numerous steps in sample preparation wherein cells are suspended prior to downstream steps such as lysis, permeabilizing or sorting, followed by performing assays such as telomerase detection in extracts or intact cells, one particular method is removal of cells from a tumor through a fine needle, as taught by Harley (column 24, lines 26-35). In this case, cells are drawn though a fine needle, which is known to have the effect of breaking cell aggregates and will suspend at least some of the cells. Therefore, at least some of the suspended cells will be passed through the fine needle at least once, even if they were originally in aggregated form. The purpose of the needle biopsy is not necessarily to break up the aggregates, but rather to remove the cells from a tumor, but the effect of passing through the needle will suspend at least some of the cells.

Finally, Applicant argues that none of the cited references teach a method comprising the step of elongating the extended product at the 3' end by one of polyadenylation and ligation, as cited in claims 6 and 15. Applicant argues that Harley teaches methods of extension of primers annealed to telomerase extension products rather than further extension of the extension products. Applicant also argues that Harley does not teach elongation by polyadenylation. Harley teaches elongation of primers annealed to elongation products by a DNA ligage, as stated in the rejection (Harley, column 9, lines 37-52). There is no requirement in the claims that both polyadenylation and ligation be used for further extension, but rather one of polyadenylation and ligation. Furthermore, while primers are in fact annealed to the extension products during polymerase or ligase chain reaction amplification of extension products, the 3' end of the extension products are extended during the amplification reaction and therefore the requirements of the claims are met. For instance, amplification can be performed by a combination of a DNA ligase and polymerase to produce identical copies identical copies of the original extended telomerase substrate (Harley, column 17, lines 49-51). That the 3' end of telomerase extension products are indeed extended during an amplification process is demonstrated by Elmore wherein the 3' end is extended to remove the hairpin structure of a labeled primer (see Figure 1).

Therefore, for the reasons stated above, the 103(a) rejections of claims 1-6, 8-13 and 15 over Harley in view of Elmore and the rejection of claims 7 and 14 over Harley in view of Elmore and further in view of Choo is maintained.

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# Summary

8. Claims 1-15 and 20 are rejected. No claims are allowable.

### Conclusion

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

### Correspondence

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David C. Thomas whose telephone number is 571-272-3320 and whose fax number is 571-273-3320. The examiner can normally be reached on 5 days, 9-5:30.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David C. Thomas Patent Examiner Art Unit 1637

/Young J. Kim/ Primary Examiner Art Unit 1637 Technology Center 1600